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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

PATENT

In re application of: Zuckermann, et al.

Application No.: 09/704,422

Filed: November 1, 2000

Title: BIOLOGICAL SAMPLE COMPONENT PURIFICATION AND DIFFERENTIAL DISPLAY

Attorney Docket No.: 1613.003/CHIRP012

Examiner: Padmanabhan, K.

Group: 1641

DECLARATION UNDER 37 CFR § 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Ronald Zuckermann, declare as follows:

1. I am a co-inventor of the above-identified patent application.

2. I earned a Ph.D. in Organic Chemistry from the University of California, Berkeley in 1989. I have served on the editorial boards of the refereed scientific journals "Molecular Diversity" and "Combinatorial Chemistry and High Throughput Screening" since 1995 and 1996, respectively. I am a co-inventor on twelve issued U.S. patents and a coauthor of over fifty published papers in the fields of organic and bioorganic chemistry.

3. I have worked as a research scientist at Chiron Corporation since 1989, and I currently hold the position of Director of Bioorganic Chemistry at Chiron Technologies, Chiron Corporation, Emeryville, CA (hereinafter "Chiron").

4. Throughout the 1990's, my research group at Chiron was working on enhancements to substrates useful in a variety of chemical processes, including solid phase chemical synthesis, screening and separation techniques. In March of 1997, my co-worker, Fred Cohen, and I filed U.S. Patent Application No. 08/828,195 directed to some of these enhancements. A Patent Cooperation Treaty (PCT) application claiming priority to Application No. 08/828,195 was filed in March of 1998. I understand that that PCT application, having International Publication Number WO 98/42730, has

been cited by the Examiner of the present application in rejecting the above-identified patent application on the grounds that it renders the invention claimed therein obvious. I disagree.

5. The aspect of the invention presently claimed in the above-identified application is directed to a method for providing a biological sample component expression pattern for a biological sample. The method involves applying a biological sample to an affinity support composed of one or more ligands coupled to a biological sample-compatible matrix. As noted in the Summary section of the application at page 5, lines 1-19, in particular lines 1-4, and in the Detailed Description section of the application at page 10, line 15 to page 11, line 12, in particular page 10, line 16 to page 11, line 5, the affinity support materials of the invention have binding affinities characterized by intermediate specificities for biological sample components, as opposed to the very general or specific binding characteristics of conventional affinity support materials.

6. Our work described in the PCT application (WO 98/42730) cited by the Examiner describes a substrate and technique for functionalizing that substrate to conduct screening of biological samples. It does not address the character of the ligands with which the substrate is functionalized in any categorical way relating to affinity/specificity. The PCT application was focused on a substrate that can be used in either aqueous or organic media and a technique for functionalizing that substrate. It does not provide any disclosure relating to the affinity/specificity characteristics of the binding between the ligands with which the substrate is functionalized and the samples run on that substrate that would teach or suggest the supports with ligands having binding affinity characterized by intermediate specificity of the invention described and claimed in the present application. As a result, I do not believe that a person of skill in the art to which this invention pertains would consider the PCT application applicable to this important aspect of the present invention, and certainly not to render the invention of the present application obvious.

7. I also understand that the Examiner of the present application has raised the concern that the term "intermediate" is indefinite as used in claim 1 as it was pending at the time of the most recent Office Action and, as such, would not reasonably apprise one of ordinary skill in the art of the scope of the invention we claim. The claim has been amended in an effort to clarify that which is intended by the "intermediate" term. The ligands used in the supports of the present invention have binding characteristics that are intermediate in nature between those of the supports used in conventional separation techniques. The binding characteristics of conventional ligands and the

ligands of the present invention are described in the specification of the present application with reference to their binding affinity and specificity (e.g., at page 1, line 15 to page 2, line 12; and at page 10, line 15 to page 11, line 12). As noted therein, the ligands of the present invention are composed of a plurality of affinity property groups and hydrophilic groups pendent from a backbone and are configured to at least partially resolve at least one component of a biological sample applied to the support comprising the ligands. The combination of multiple ligand constituents having different affinity characteristics allows for the tailoring of ligands that have greater specificity for a particular component or components of a biological sample than conventional general chromatography resin ligands (e.g., cations or anions (charge-based)), but less specificity than conventional affinity support ligands directed to a specific target or antigen (e.g., antibodies or antibody fragments (antibody-based)). This important feature of the ligands used in the supports of the present invention distinguishes them from those conventionally used on the basis that they have a binding affinity, or specificity, for a particular component(s) of a biological sample that is intermediate between the extremes characteristic of the ligands of the conventional very general or very specific supports previously available. The recitation in amended claim 1 of "said ligand having a binding affinity characterized by a specificity for a component of a biological sample that is intermediate between charge-based and antibody-based ligands" refers to this important and distinguishing feature and would, I believe, be clear and readily understood by those of skill in the art to which this invention pertains.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true. I further declare that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both (under Section 1001 of Title 18 of the United States Code), and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Ronald N. Zuckermann

6/23/03

Date